NATIONAL CANCER INSTITUTE

CLINICAL TRIALS AND TRANSLATIONAL RESEARCH ADVISORY COMMITTEE

PROGRESS IN SMALL CELL LUNG CANCER RESEARCH WORKING GROUP

Working Group Report, July 2016

INTRODUCTION

On September 19, 2012, the 112th Congress amended the Public Health Service Act by enacting the Recalcitrant Cancer Research Act (RCRA) of 2012[1]. The legislation called upon the National Cancer Institute (NCI) to identify two or more recalcitrant cancers that "have a 5-year relative survival rate of less than 20 percent" and "cause the death of at least 30,000 individuals in the United States per year"; and to, "develop … scientific framework(s) for the conduct or support of research on such cancer(s)." Small cell lung cancer (SCLC) is a recalcitrant cancer as defined by its five-year relative survival rate of less than seven percent and the loss of approximately 30,000 lives per year. The NCI's scientific framework for SCLC[2] was submitted to Congress in June 2014 and posted on NCI's website. In January 2016, the NCI convened the Progress in SCLC Research Working Group (SCLC Progress WG), chaired by Dr. Charles Rudin, Chief, Thoracic Oncology, Memorial Sloan Kettering Cancer Center (MSKCC), to advise NCI on the progress of the research initiatives outlined in the scientific framework. The working group members represent the broad clinical and translational research and advocacy communities (Appendix 1).

The working group's main objectives are to:

1. Assess the research progress and identify new scientific opportunities related to the initiatives in the scientific framework for SCLC;
2. Provide recommendations for the process to be used for future assessments;
3. Review and provide recommendations for updating the scientific framework no later than five years after its initial development;
4. Advise the NCI on the effectiveness of the scientific framework no later than six years after its initial development.

This report summarizes the initial assessment of the working group.

THE SCIENTIFIC INITIATIVES

The 2014 scientific framework for SCLC provides the background, rationale, and implementation plans for five initiatives proposed to expand SCLC research. These initiatives are summarized below:

1. **Better Research Tools for the Study of SCLC.** Build better research tools for the study of SCLC by (a) optimizing the collection of tumor tissue specimens representing distinct phases of SCLC (from initial diagnosis to disease recurrence following radio-chemotherapy) and (b) developing new tumor models (e.g., cell lines, patient-derived xenografts, and genetically-engineered mouse models) that reflect the phases of SCLC found in the clinic.

2. **Comprehensive Genomic Profiling of SCLC.** Expand comprehensive genomic profiling studies of clinically-annotated SCLC specimens to improve the basic understanding of the frequency, distribution, and range of molecular abnormalities that exist both at diagnosis and following therapeutic relapse.

3. **New Diagnostic Approaches for SCLC.** Investigate new diagnostic approaches for populations at high risk of developing SCLC.

4. **Therapeutic Development Efforts.** Focus therapeutic development efforts on specific molecular vulnerabilities of SCLC (tumor suppressor genes, unique genetic drivers and their pathways, neuronal characteristics, and immunotherapy).

5. **Mechanisms Underlying Both High Rate of Initial Response and Rapid Emergence of Drug and Radiation Resistance.** Examine the mechanisms underlying both the high initial rate of response to primary SCLC therapy and the rapid emergence of drug and radiation resistance following completion of treatment.

ASSESSMENT OF RESEARCH PROGRESS

A summary and abstracts of Fiscal Year 2014 NCI extramural grants, cooperative agreements, and intramural programs relevant to SCLC, as well as extramural grants from other NIH institutes and NCI-supported clinical trials were reviewed by the working group (Appendix 2).

The working group convened via webinar in April 2016 to discuss progress in the initiatives defined within the scientific framework, remaining gaps, and recommendations to facilitate continued progress.

SUMMARY OF PROGRESS FOR THE SCIENTIFIC INITIATIVES

The 2014 scientific framework for SCLC provides the background, rationale, and implementation plans for five initiatives proposed to expand SCLC research. The initiatives, implementation plans, and progress assessments are summarized below.

INITIATIVE 1: BETTER RESEARCH TOOLS FOR THE STUDY OF SCLC

Build better research tools for the study of SCLC by (a) optimizing the collection of tumor tissue specimens representing distinct phases of SCLC (from initial diagnosis to disease recurrence following radio-chemotherapy) and (b) developing new tumor models (e.g., cell lines, patient-derived xenografts, and genetically-engineered mouse models) that reflect the phases of SCLC found in the clinic.

SCLC is routinely diagnosed with biopsies obtained via fine needle aspirate and hence a paucity of material is available for research purposes. Moreover, additional tumor models, including clinically-annotated cell lines derived from SCLC patients, patient-derived xenografts (PDX), and genetically-engineered mouse models (GEMM) that represent different aspects of the human disease, such as resistant and recurrent disease models, are required.

Recent initiatives, including the Patient-Derived Models (PDM) Repository and administrative supplements given to NCI-supported cancer centers to increase the number of surgical and blood specimens available for model development, were recognized in the scientific framework and expansion of these efforts was encouraged.

To address these gaps in research tools, the NCI proposed an implementation plan to: support infrastructure for SCLC specimen collection over the next 3 years, fund collaborative projects across NCI's research networks to expand the generation of PDXs and cell lines, and obtain specimens from biopsies of SCLC patients enrolled in clinical trials or for whom detailed clinical information is available.

Assessment: Implementation is on target; SCLC model development has advanced considerably since the drafting of the scientific framework, but it is too early to assess scientific progress.

Activities to date:

In December 2015, the NCI released a series of program announcements with special review (PARs; PAR-16-049[3], PAR-16-050[4], and PAR-16-051[5]) to support and establish the SCLC Consortium, which is intended to address all five of the initiatives from the scientific framework. With respect to Initiative 1, the Coordinating Center for the SCLC Consortium (PAR-16-050) will secure centralized tissue banking for specimens submitted by the members of the SCLC Consortium, create a virtual biospecimen database that would include all tissue resources of the SCLC Consortium, and establish SCLC in vivo and in vitro model repositories and distribution units. The first receipt date for applications was in March 2016 with review expected to occur in July 2016. Each PAR has additional receipt dates.

The NCI PDM Repository at the Frederick National Laboratory for Cancer Research (FNLCR) has been created to establish and provide PDX models, frozen tumor fragments, and cultured cells from patient tumors and circulating tumor cells (CTCs). Anticipated resources include DNA and RNA pellets from PDXs, CTC-derived xenografts (CDX), and primary cell lines; and 70 human SCLC cell lines with associated array and screening data. The PDM Repository is currently receiving tissue (resections, biopsies) and blood samples for CTC enrichment from two NCI clinics, 16 comprehensive cancer centers, and 23 NCI Experimental Therapeutics Clinical Trials Network (ETCTN) and NCI Community Oncology Research

Program (NCORP) centers. In addition to the support given to cancer centers noted above, the NCI has provided supplemental funding to NCORP sites for biospecimen collection for the PDM Repository, with an emphasis on SCLC samples. SCLC specimens received to date from these sources include one resection, one malignant effusion, and 121 blood specimens. The PDM Repository currently has three histologically confirmed SCLC PDX models (one from tissue, one from pleural fluid, and one from CTCs) that are being developed and characterized for future distribution.

Many other groups have begun to make PDX models routinely. MD Anderson Cancer Center, MSKCC, and Massachusetts General Hospital have protocols in place for the generation of PDXs and CDXs. CDXs in particular have emerged as important models[6], and CTC-derived cell lines are being generated as well at multiple centers.

The NCI and the International Association for the Study of Lung Cancer (IASLC) conducted an assessment of available SCLC research resources (presented at the 2015 IASLC SCLC Workshop) in an effort to enhance sharing of these resources across the international SCLC research community.

New GEMMs are also emerging that are providing important insights, including the role of *ASCL1* and other key determinants[7,8].

Recommendations:

- Remain committed to the SCLC Consortium over multiple funding cycles (applies generally to all five initiatives).
- Create and maintain clinically-annotated tissue microarrays (TMA) at NCI and other centers for use by the research community.
- Work with the National Clinical Trial Network (NCTN) Groups and with community and academic centers to enhance and coordinate biospecimen collection.
- Facilitate sharing of SCLC samples, genomics data, and other research resources and make them available quickly.
- Clearly there is an urgent need to coordinate efforts to obtain clinically informed biospecimens from SCLC patients to facilitate development and characterization of new SCLC preclinical models. As progress is reviewed and if it is found inadequate, it may be necessary for the NCI to begin a more intensive coordinated effort at such collection.

INITIATIVE 2: COMPREHENSIVE GENOMIC PROFILING OF SCLC

Expand comprehensive genomic profiling studies of clinically-annotated SCLC specimens to improve the basic understanding of the frequency, distribution, and range of molecular abnormalities that exist both at diagnosis and following therapeutic relapse.

Genomic studies of SCLC have confirmed the near ubiquitous loss of *TP53* and *RB* function in SCLC tumors, activation of *MYC* genes, and have identified potential oncogenic drivers such as *SOX2* amplification and *PTEN* loss[9,10]. However, the number of tumors characterized in these initial studies is

not sufficient to identify low-prevalence mutations, and comparative comprehensive genomic analyses of chemo-sensitive, chemo-resistant, and metastatic disease are still important priorities. Increased, coordinated sample acquisition from the cancer centers and NCI-supported clinical trials will enable additional studies that will increase the total number of evaluated tumors.

To achieve the goals, the NCI proposed an implementation plan to: characterize the genetic and molecular features of the SCLC specimens that have been collected at diagnosis and relapse over the next 3 to 5 years.

Assessment: Implementation is on target; it is too early to assess scientific progress.

Activities to date:

The NCI released a PAR in December 2015 for the SCLC Consortium Coordinating Center (PAR-16-050). In addition to the objectives defined in the previous section, the Coordinating Center will create and support database(s) for -omics or other data pertinent to the SCLC Consortium and provide centralized biostatistics, bioinformatics and data analysis support. Projects that are supported by the individual U01 sites (PAR-16-049 and PAR-16-051) are anticipated to include molecular characterization and identification of therapeutic targets, risk factors, and molecular signatures; and -omics data obtained by such projects will be shared with the Coordinating Center.

Recent important manuscripts on SCLC genomic profiling[11-13] have added to the total number of tumors that have been analyzed and have identified potentially targetable pathways in SCLC such as Notch, the AKT/mTOR pathway, and epigenetic regulatory mechanisms. A recent investigation of the SCLC methylome has revealed a potential role for EZH2 in tumor growth[14].

Recommendations:

- Provide a central facility for next-generation sequencing at the NCI.
- Support the collection of clinically-annotated specimens for genomic studies from paired de novo and recurrent disease, as well as from primary and metastatic sites, including post-mortem collection.
- Prioritize the characterization of “typical” SCLC genomes (i.e., not early-stage disease).
- Encourage studies of clinically-defined subsets from clinical trials such as responders vs. non-responders and exceptional responders.

INITIATIVE 3: NEW DIAGNOSTIC APPROACHES FOR SCLC

Investigate new diagnostic approaches for populations at high risk of developing SCLC.

New approaches for the diagnosis, screening, and early detection of SCLC are needed. Of the SCLC cases detected in the National Lung Screening Trial, the vast majority were extensive-stage disease, indicating that neither chest radiography nor low-dose helical computed tomography are effective screening tools for early detection of SCLC[15]. Tissue-, blood-, and sputum-based methods that take advantage of the

genetic characteristics of SCLC (*TP53* and *RB* mutations, neuroendocrine lineage markers such as *ASCL1*) may lead to improvements. Recent technical advances in blood-based tumor detection may also represent new opportunities for screening methodologies[6,16].

The implementation plan proposed by the NCI was to: issue a Program Announcement in the second half of 2015 and support studies focused on discovering early molecular changes in histologically normal lung, blood (including circulating DNA), and other relevant tissues that could be applied to subsequent screening studies in high risk populations.

Assessment: Implementation is on target; it is too early to assess scientific progress.

Activities to date:

As part of the December 2015 NCI funding announcement for the SCLC Consortium, PAR-16-051 will support individual U01 sites for "Innovative Approaches to the Prevention and Early Detection of SCLC", to conduct studies to expand the understanding of the critical molecular changes in the lung that precede the development of frank SCLC; and/or to identify populations at particularly high risk for SCLC. The U01 sites will share data, materials, models, and results with the Coordinating Center, which will support the administrative coordination of the SCLC Consortium.

Recommendations:

- Support additional focused projects for early detection

INITIATIVE 4: THERAPEUTIC DEVELOPMENT EFFORTS

Focus therapeutic development efforts on specific molecular vulnerabilities of SCLC (tumor suppressor genes, unique genetic drivers and their pathways, neuronal characteristics, and immunotherapy).

The ASCL1, MYC, and Notch signaling pathways represent potentially targetable lesions in SCLC. Continued efforts in the development of therapeutics targeted to components of these pathways may bear fruit. Although the restoration of tumor suppressor function is not currently feasible, studies aimed at uncovering synthetic lethality associated with the loss of TP53 and RB function may reveal new targets for SCLC therapy. In addition, recent evidence of response to immune checkpoint inhibitors in SCLC patients is highly promising.

Assessment: Implementation is on target; it is too early to assess scientific progress.

Activities to date and Recommendations: Please see consolidated summary under Initiative 5 below.

INITIATIVE 5: MECHANISMS OF INITIAL RESPONSE AND EMERGENCE OF RESISTANCE

Examine the mechanisms underlying both the high initial rate of response to primary SCLC therapy and the rapid emergence of drug and radiation resistance following completion of treatment.

The rapid acquisition of resistance to both chemo- and radiation therapy is a common feature of SCLC and appears to occur through a variety of mechanisms including elevated expression of DNA repair and ABC transporter proteins, activation of the PI3K/AKT/mTOR pathway, and expression of stem cell markers, among others. Definitive molecular characterization of the primary mechanisms of acquired resistance will require access to a greater number of clinical samples and the development of new model systems.

To address both of the goals of therapeutic development and mechanisms of initial response and emergence of resistance, the NCI proposed an implementation plan to: issue a Program Announcement in the second half of 2015, supporting studies focused on understanding the unique features of SCLC that could be used to develop new therapeutics, identify molecular vulnerabilities that could be used to develop target agent combinations, and understand the high rate of initial response and rapid development of clinical resistance to drug and radiation therapy.

Assessment: Implementation is on target; it is too early to assess scientific progress.

Activities to date:

As part of the December 2015 NCI funding announcement for the SCLC Consortium, PAR-16-049 will support individual U01 sites for "Therapeutic Development and Mechanisms of Resistance" to conduct preclinical studies to improve SCLC therapeutics, focusing on understanding how the molecular vulnerabilities of this cancer could be used to develop targeted agent combinations; and/or to gain a better understanding of the rapid development of clinical resistance to drug and radiation therapy. The U01 sites will share data, materials, models, and results with the Coordinating Center, which will support the administrative coordination of the SCLC Consortium.

The FNLCR executed high-throughput screening of approved and investigational drugs against a panel of SCLC cell lines[17].

The NCI Cancer Therapy Evaluation Program (CTEP) sponsored a meeting on May 8, 2015 in Rockville, MD to discuss opportunities for biomarker-driven trials in SCLC. This meeting expanded on ideas discussed at the IASLC SCLC Workshop the prior month. Participants included representatives from all of the NCTN Groups.

The NCI Thoracic Malignancy Steering Committee made the "rapid testing of new agents and strategies for the treatment of (SCLC)" one of its strategic priorities for 2015.

Recent publications have provided new insights into mechanisms of PARP inhibitor sensitivity[18,19] and notable clinical advances, including substantial responses to immunotherapy[20] and a DLL3-directed antibody-drug conjugate[21], have been reported. New therapeutic approaches and drugs that target

"transcriptional addictions" in SCLC are also being discovered and need to be tested in preclinical models and subsequently in the clinic[22-25].

Recommendations:

- Continue to engage with the NCTN and ETCTN to develop biomarker-driven trials for SCLC.
- Work with the NCTN Groups and with community and academic centers to accelerate accrual to trials.
- Consider the inclusion of non-pulmonary small cell histologies in SCLC trials.
- Emphasize inclusion of less common subsets of patients, such as non-smokers.

OTHER ACTIVITIES RELEVANT TO SCLC

To engage the research community in continuing the research agenda described in the scientific framework and to identify new research opportunities, the NCI proposed a joint workshop with the IASLC in early 2015. The IASLC Small Cell Lung Cancer Workshop was held on April 22-24, 2015 at MSKCC. This forum brought 200 investigators from the international research community together in what was the largest meeting focused solely on SCLC in many years[26]. NCI scientific and program staff took part in the meeting and helped in its organization.

NCI staff members, along with other scientists and advocates, participated in the *FasterCures* Small Cell Lung Cancer Action Plan Meeting in May 2015 in Chicago, IL to discuss challenges and opportunities in SCLC[27].

The Cancer Clinical Investigator Team Leader Award (CCITLA)[28] was modified in 2015 to encourage applications with candidates with a research focus on recalcitrant cancers, including SCLC. Awardees with a focus on SCLC have included Dr. Leora Horn of Vanderbilt-Ingram Cancer Center and Dr. Liza Villaruz of the University of Pittsburgh Cancer Institute in 2015, and Dr. Taofeek Owonikoko of Winship Cancer Institute of Emory University in 2016.

Recommendations:

- Organize additional meetings like the April 2015 IASLC SCLC workshop, possibly in conjunction with SCLC Consortium meetings.
- Organize/promote SCLC-focused sessions at major meetings (AACR, ASCO, EORTC-NCI-AACR Molecular Targets, etc.).
- Partner with lung cancer advocacy groups to publicize SCLC research and promote clinical trial accrual.
- Partner with lung cancer foundations to share a consensus on high priority research areas in SCLC.
- Provide career development awards for SCLC investigators.

CONCLUSIONS AND NEXT STEPS

The working group concluded that the five initiatives outlined in the scientific framework remain relevant. Implementation of the initiatives to date is progressing according to plan and, although it is too early to assess scientific progress resulting from these initiatives, a number of important scientific papers have been published since the development of the scientific framework that describe important advances in CDX models, the genomic landscape of SCLC, and mechanisms of PARP inhibitor sensitivity in SCLC. Moreover, recent developments in clinical trials of checkpoint inhibitors and an antibody-drug conjugate show promise. It was noted that there was insufficient attention to radiation therapy in the initial development of the scientific framework. Greater emphasis should be placed on this modality in future assessments and in a revised framework.

The working group will continue to periodically review information about NIH/NCI programs and initiatives, grants, projects, contracts, and clinical trials associated with each of the initiatives. The working group recommended that the next assessment should be scheduled for early 2018, approximately one year after the first round of awards are made for the SCLC Consortium Coordinating Center and individual U01 sites. The plan is to provide a progress report to CTAC on an annual or biennial basis focusing on implementation and scientific progress. In addition, the working group will review and provide recommendations for updating the scientific framework no later than June 2019 and advise NCI on the effectiveness of the scientific framework no later than June 2020 (i.e., five and six years after the initial development of the scientific framework).

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APPENDICES - SUPPLEMENTAL RESOURCES

Appendix 1: Progress in Small Cell Lung Cancer Research Working Group Roster

Appendix 2: NIH Investments in Small Cell Lung Cancer Research

APPENDIX 1: NATIONAL CANCER INSTITUTE CLINICAL TRIALS AND TRANSLATIONAL RESEARCH ADVISORY COMMITTEE – PROGRESS IN SMALL CELL LUNG CANCER RESEARCH WORKING GROUP ROSTER

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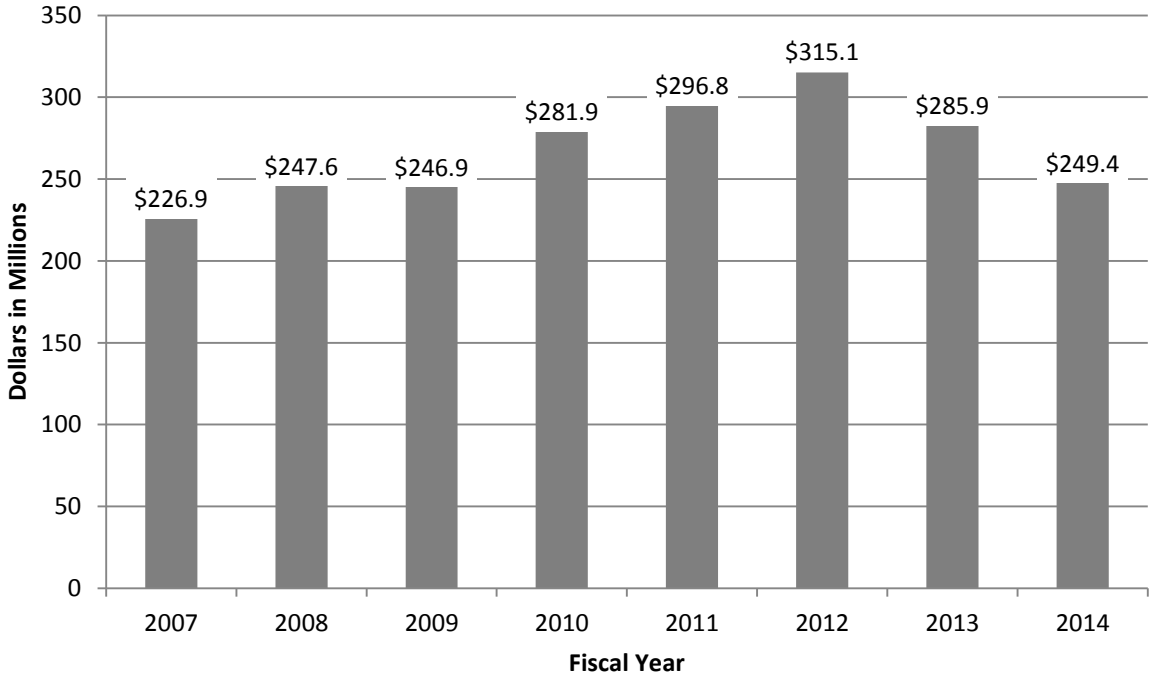
APPENDIX 2: NCI INVESTMENTS IN SMALL CELL LUNG CANCER RESEARCH

NCI Investments in Lung Cancer Research

In fiscal year 2014 (FY 2014), the National Cancer Institute (NCI) invested $249.4 M in lung cancer research (see Figure 1). Funding numbers from FY 2007-FY 2013 were obtained from the NCI Funded Research Portfolio.

Figure 1. NCI Lung Cancer Research Investment



NIH Investments in Small Cell Lung Cancer Research

Analysis of the FY 2014 NCI lung cancer research portfolio yielded 17 projects with a focus on small cell lung cancer (SCLC) (Table 1). These projects include NCI extramural grants, cooperative agreements, and intramural programs. Analysis of the NIH lung cancer research portfolio yielded four additional projects (Table 2); all are extramural grants from other institutes. Clinical Trials are summarized separately in the *Clinical Trials* section; some may be included in Table 1 if they are funded by an individual grant. The project numbers in the tables are hyperlinked to NIH RePORTER, where one can access the abstracts and other information of interest.

Extramural projects were identified as relevant to SCLC by the NCI Division of Extramural Activities Research Analysis and Evaluation Branch (RAEB) and then matched with a term search of application abstracts and specific aims, followed by a manual review of entire applications, if necessary. Intramural projects coded for Lung Cancer were reviewed manually, and then compared to a term search of project descriptions.

SCLC research projects from other NIH ICs were identified by text mining and matching to the NIH Research, Condition, and Disease Categorization (RCDC) thesaurus terms "lung small cell carcinoma" or "lung neuroendocrine carcinoma". All four projects are in the NIH RCDC Lung Cancer category.

Table 1. FY 2014 NCI-Funded Projects Related to Small Cell Lung Cancer

Type	Project Number	Title	Contact PI	Institution
5	F32CA165856-03	Understanding the role of SKP2 in small cell lung cancer progression	Nicolay, Brandon	Massachusetts General Hospital
5	K23CA164015-04	Novel systemic therapy to improve clinical outcome in small cell lung cancer	Owonikoko, Taofeek K.	Emory University
2	P50CA058187-19A1	SPORE in Lung Cancer	Bunn, Paul	University of Colorado, Denver
5	R01CA112557-09	Molecular Mechanisms of Nickel-induced Tumorigenicity.	Huang, Chuanshu	New York University School of Medicine
5	R01CA136534-05	Structure-based anti-cancer drug development	Deng, Xingming	Emory University
5	R01CA138759-05	Stat3 Downstream Genes as Lung Adenocarcinoma Biomarkers	Yan, Cong	Indiana Univ-Purdue Univ at Indianapolis
5	R01CA148867-06	Using mouse models to understand retinoblastoma initiation and progression	Macpherson, David	Fred Hutchinson Cancer Research Center
5	R01CA152316-04	Discovery of novel PCFT-targeted agents	Matherly, Larry H.	Wayne State University
5	R01CA170386-03	Novel Pathogen Associated Cancers (PQ12)	Galloway, Denise A.	Fred Hutchinson Cancer Research Center
5	R21CA169979-02	ACTIVITY-BASED KINASE DISCOVERY IN SMALL CELL LUNG CANCER	Haura, Eric B.	H. Lee Moffitt Cancer Ctr & Res Inst

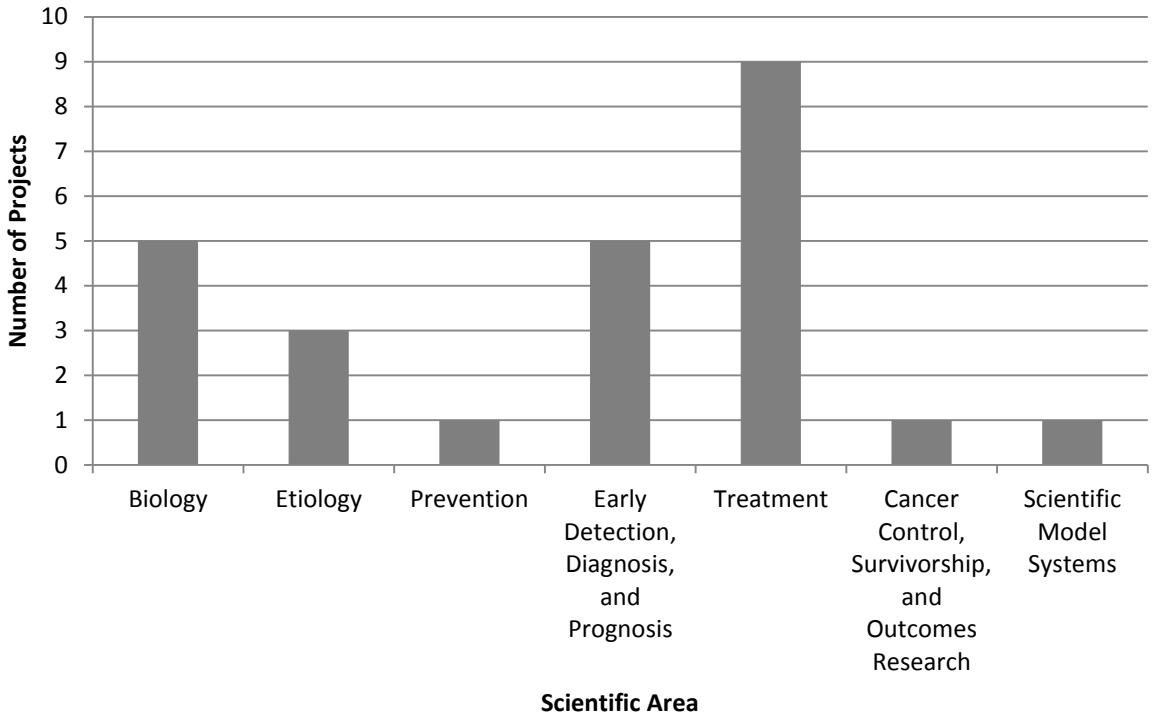
Type	Project Number	Title	Contact PI	Institution
1	R43CA177025-01A1	Synergy between MAG-1 and Cyclophosphamide for Treatment of Recurrent SCLC	Pang, Roy H.L.	Woomera Therapeutics, Inc.
4	R44CA174074-02	Development of GZ38-1, a Novel Protectant of Chemotherapy-Induced Myelosuppressio	Strum, Jay Copeland	G1 Therapeutics, Inc.
5	U01CA151452-05	COMBINATORIAL-DESIGNED NANO-PLATFORMS TO OVERCOME TUMOR DRUG RESISTANCE	Amiji, Mansoor M.	Northeastern University
5	U54CA151838-05	Center of Cancer Nanotechnology Excellence at Johns Hopkins	Searson, Peter C.	Johns Hopkins University
5	U54CA151881-05	Center for Translational Cancer Nanomedicine	Torchilin, Vladimir P	Northeastern University
	ZIABC010448-13	Genetic Alterations in Lung Cancer	Wiest, Jonathan Scott	National Cancer Institute
	ZIASC000167-23	Molecular Pathology of Pulmonary Carcinogenesis	Linnoila, Ilona	National Cancer Institute

Table 2. FY 2014 Non-NCI NIH Funded Projects Related to Small Cell Lung Cancer

Type	Project Number	Title	Contact PI	Institution
5	R01GM079719-08	Enabling new translational discoveries using a genomic data-driven nosology	Butte, Atul J.	Stanford University
5	R21AG042894-02	Translational meta-analysis for elderly lung cancer patients	Wang, Xiaofei	Duke University
1	R21AG047175-01	Comparative Effectiveness of Treatment Regimens in Lung Cancer	Lamont, Elizabeth B	Harvard Medical School
5	R01HL115207-02	The lineage and function of neuroendocrine cells in lung homeostasis and injury	Chuang, Pao-Tien	University of California, San Francisco

Each NCI project is categorized (by RAEB and the NCI Intramural divisions) around seven broad areas of scientific interest in cancer research, defined and classified according to the Common Scientific Outline (CSO). The distribution of FY 2014 SCLC projects is shown in Figure 2. Projects may be relevant multiple scientific areas, and thus may be represented more than once in Figure 2.

Figure 2. FY 2014 NCI-Funded Small Cell Lung Cancer Projects by Scientific Area



Workforce Development in SCLC Research

NCI supports training and career development through a variety of activities. NCI-supported training and career development grants relevant to SCLC in FY 14 are in Table 3. In addition, the NCI gives the Cancer Clinical Investigator Team Leadership Awards (CCITLA), to recognize and support outstanding clinical investigators at NCI-designated Cancer Centers who are actively engaged in NCI-funded collaborative clinical trials. These awards are also designed to promote the retention of clinical investigators in academic research careers. Two 2015 CCITLA recipients focus on small cell lung cancer: Leora Horn, M.D., M.Sc., of Vanderbilt-Ingram Cancer Center; and Liza Villaruz, M.D., of the University of Pittsburgh Cancer Institute.

Table 3. FY 2014 Training and Career Development Awards

Type	Project Number	Title	Contact PI	Institution
5	F32CA165856-03	Understanding the role of SKP2 in small cell lung cancer progression	Nicolay, Brandon	Massachusetts General Hospital
5	K23CA164015-04	Novel systemic therapy to improve clinical outcome in small cell lung cancer	Owonikoko, Taofeek K.	Emory University

Clinical Trials

As of February 2016, 79 interventional clinical trials in SCLC with NCI involvement were ongoing or recently completed. A search for interventional trials for the condition "small cell lung cancer" was performed on clinicaltrials.gov on February 8, 2016. Trials with known status and performed by an NCI-supported group or network, at the NIH clinical center, or at an NCI-designated cancer center are included in the list. Trials completed prior to January 2015 are not included. A list of these clinical trials is in Table 4. The NCT numbers in the table are hyperlinked to ClinicalTrials.gov.

Table 4. Clinical trials related to SCLC

NCT Number	Title	Sponsor	Phases	Primary Purpose
NCT00009971	Fenretinide in Treating Patients With Recurrent Small Cell Lung Cancer	National Cancer Institute (NCI)	Phase 2	Treatment
NCT00084799	Monoclonal Antibody Therapy in Treating Patients With Progressive Small Cell Lung Cancer	Ludwig Institute for Cancer Research	Phase 1	Treatment
NCT00310141	Computer-Assisted Counseling in Helping African American Smokers Stop Smoking	M.D. Anderson Cancer Center	not applicable	Prevention

NCT Number	Title	Sponsor	Phases	Primary Purpose
NCT00363428	Lung Rehabilitation in Treating Patients With Chronic Obstructive Pulmonary Disease Who Are Undergoing Surgery for Lung Cancer	Mayo Clinic	Phase 2	Supportive Care
NCT00445965	Iodine I 131 Monoclonal Antibody 3F8 in Treating Patients With Central Nervous System Cancer or Leptomeningeal Cancer	Memorial Sloan Kettering Cancer Center	Phase 2	Treatment
NCT00453154	Cisplatin or Carboplatin, and Etoposide With or Without Sunitinib Malate in Treating Patients With Extensive-Stage Small Cell Lung Cancer	National Cancer Institute (NCI)	Phase 1|Phase 2	Treatment
NCT00554463	G-CSF and Pegfilgrastim in Treating Neutropenia in Patients Undergoing Radiation Therapy and Chemotherapy for Limited Stage Small Cell Lung Cancer	Radiation Therapy Oncology Group	Phase 2	Supportive Care
NCT00613626	Cisplatin + Etoposide +/- Concurrent ZD6474 in Previously Untreated Extensive Stage Small Cell Lung Cancer	Hoosier Cancer Research Network	Phase 2	Treatment
NCT00617409	To Immunize Patients With Extensive Stage SCLC Combined With Chemo With or Without All Trans Retinoic Acid	H. Lee Moffitt Cancer Center and Research Institute	Phase 2	Treatment
NCT00632853	Radiation Therapy Regimens in Treating Patients With Limited-Stage Small Cell Lung Cancer Receiving Cisplatin and Etoposide	Alliance for Clinical Trials in Oncology	Phase 3	Treatment

NCT Number	Title	Sponsor	Phases	Primary Purpose
NCT00765973	Topotecan Liposomes Injection for Small Cell Lung Cancer (SCLC), Ovarian Cancer and Other Advanced Solid Tumors	Spectrum Pharmaceuticals, Inc	Phase 1	Treatment
NCT00807755	Everolimus, Carboplatin, and Etoposide in Treating Patients With Small Cell Lung Cancer or Other Advanced Solid Tumors	University of California, Davis	Phase 1	Treatment
NCT00828139	Topotecan With or Without Aflibercept in Treating Patients With Extensive-Stage Small Cell Lung Cancer	National Cancer Institute (NCI)	Phase 2	Treatment
NCT00856037	Topotecan Hydrochloride and Doxorubicin Hydrochloride in Treating Patients With Small Cell Lung Cancer That Has Relapsed or Not Responded to Treatment	University of Nebraska	Phase 1	Treatment
NCT00856830	Bendamustine With Irinotecan Followed by Etoposide/Carboplatin for Patients With Extensive Stage Small Cell Lung Cancer	University of Alabama at Birmingham	Phase 1|Phase 2	Treatment
NCT00887159	Cisplatin and Etoposide With or Without Vismodegib or Cixutumumab in Treating Patients With Extensive-Stage Small Cell Lung Cancer	National Cancer Institute (NCI)	Phase 2	Treatment
NCT00921739	Esophageal Sparing Intensity-modulated Radiation Therapy (IMRT) for Locally-Advanced Thoracic Malignancies	Duke University	Phase 1	Treatment

NCT Number	Title	Sponsor	Phases	Primary Purpose
NCT00926640	A Phase I Study of Belinostat in Combination With Cisplatin and Etoposide in Adults With Small Cell Lung Carcinoma and Other Advanced Cancers	National Cancer Institute (NCI	Phase 1	Treatment
NCT01017601	Seneca Valley Virus-001 After Chemotherapy in Treating Patients With Extensive-Stage Small Cell Lung Cancer	Alliance for Clinical Trials in Oncology	Phase 2	Treatment
NCT01055197	Radiation Therapy in Treating Patients With Extensive Stage Small Cell Lung Cancer	Radiation Therapy Oncology Group	Phase 2	Treatment
NCT01110226	Trial Of Cisplatin And KML-001 in Platinum Responsive Malignancies	University of Maryland	Phase 1	Treatment
NCT01165658	Hypofractionated Proton Radiation Therapy	M.D. Anderson Cancer Center	Phase 1	Treatment
NCT01237678	A Study to Test Safety and Efficacy of IMGN901 in Combination With Carboplatin/Etoposide in Patients With Advanced Solid Tumors and Extensive Stage Small Cell Lung Cancer	ImmunoGen, Inc.	Phase 1|Phase 2	Treatment
NCT01253161	Study of Pasireotide Long Acting Release (LAR) in Patients With Metastatic Neuroendocrine Tumors (NETs)	H. Lee Moffitt Cancer Center and Research Institute	Phase 2	Treatment
NCT01286987	Study of BMN 673, a PARP Inhibitor, in Patients With Advanced or Recurrent Solid Tumors	Medivation, Inc.	Phase 1	Treatment

NCT Number	Title	Sponsor	Phases	Primary Purpose
NCT01306045	Molecular Profiling and Targeted Therapy for Advanced Non-Small Cell Lung Cancer, Small Cell Lung Cancer, and Thymic Malignancies	National Cancer Institute (NCI)	Phase 2	Treatment
NCT01349647	Immunization With a Pentavalent Vaccine Composed of KLH-conjugates of GD2L, GD3L, Globo H, Fucosyl GM1, and N-Propionylated Polysialic Acid	Memorial Sloan Kettering Cancer Center	Phase 1	Treatment
NCT01450761	Trial in Extensive-Disease Small Cell Lung Cancer (ED-SCLC) Subjects Comparing Ipilimumab Plus Etoposide and Platinum Therapy to Etoposide and Platinum Therapy Alone	Bristol-Myers Squibb	Phase 3	Treatment
NCT01470248	Study of Arsenic Trioxide in Small Cell Lung Cancer	Emory University	Phase 2	Treatment
NCT01553916	Neuroprotective Effects of Lithium in Patients With Small Cell Lung Cancer Undergoing Radiation Therapy to the Brain	Washington University School of Medicine	Phase 1|Phase 2	Supportive Care
NCT01573338	Clinical Study to Evaluate the Maximum Tolerated Dose of BAY1000394 When Given Together With Chemotherapy and the Effectiveness of This Combination Treatment in Shrinking a Specific Type of Lung Tumors (Smal Cell Lung Cancer)	Bayer	Phase 1|Phase 2	Treatment

NCT Number	Title	Sponsor	Phases	Primary Purpose
NCT01579929	Combination of the Hedgehog Inhibitor, LDE225, With Etoposide and Cisplatin in the First-Line Treatment of Patients With Extensive Stage Small Cell Lung Cancer (ES-SCLC)	Memorial Sloan Kettering Cancer Center	Phase 1	Treatment
NCT01638546	Temozolomide With or Without Veliparib in Treating Patients With Relapsed or Refractory Small Cell Lung Cancer	National Cancer Institute (NCI)	Phase 2	Treatment
NCT01642251	Cisplatin and Etoposide With or Without Veliparib in Treating Patients With Extensive Stage Small Cell Lung Cancer or Metastatic Large Cell Neuroendocrine Non-small Cell Lung Cancer	National Cancer Institute (NCI)	Phase 1|Phase 2	Treatment
NCT01654965	Tivantinib and Topotecan Hydrochloride in Treating Patients With Advanced or Metastatic Solid Tumors	National Cancer Institute (NCI)	Phase 1	Treatment
NCT01722292	A Study of LY2940680 in Small Cell Lung Cancer	Eli Lilly and Company	Phase 1|Phase 2	Treatment
NCT01737502	Sirolimus and Auranofin in Treating Patients With Advanced or Recurrent Non-Small Cell Lung Cancer or Small Cell Lung Cancer	Mayo Clinic	Phase 1|Phase 2	Treatment
NCT01797159	Hippocampal Prophylactic Cranial Irradiation for Small Cell Lung Cancer	Sidney Kimmel Comprehensive Cancer Center	Phase 2	Treatment

NCT Number	Title	Sponsor	Phases	Primary Purpose
NCT01803269	Topotecan Hydrochloride or Cyclodextrin-Based Polymer-Camptothecin CRLX101 in Treating Patients With Recurrent Small Cell Lung Cancer	University of Chicago	Phase 2	Treatment
NCT01859741	A Phase 1b/2 Study of OMP-59R5 in Combination With Etoposide and Platinum Therapy in Subjects With Untreated Extensive Stage Small Cell Lung Cancer (PINNACLE)	OncoMed Pharmaceuticals, Inc.	Phase 1|Phase 2	Treatment
NCT01876446	Pegylated Irinotecan NKTR 102 in Treating Patients With Relapsed Small Cell Lung Cancer	Roswell Park Cancer Institute	Phase 2	Treatment
NCT01880528	Lisinopril in Reducing Shortness of Breath Caused by Radiation Therapy in Patients With Lung Cancer	Mayo Clinic	not applicable	Supportive Care
NCT01901653	SC16LD6.5 in Recurrent Small Cell Lung Cancer	Stemcentrx	Phase 1|Phase 2	Treatment
NCT01931787	CPI-613 in Treating Patients With Relapsed or Refractory Small Cell Lung Cancer	Comprehensive Cancer Center of Wake Forest University	Phase 1	Treatment
NCT01935336	Study of Ponatinib in Patients With Lung Cancer Preselected Using Different Candidate Predictive Biomarkers	University of Colorado, Denver	Phase 2	Treatment
NCT01941316	Study of Carfilzomib With Irinotecan in Irinotecan-Sensitive Malignancies and Small Cell Lung Cancer Patients	Cancer Research and Biostatistics Clinical Trials Consortium	Phase 1|Phase 2	Treatment

NCT Number	Title	Sponsor	Phases	Primary Purpose
NCT01987232	Phase 1b/2 Study of Carfilzomib, Carboplatin, and Etoposide in Subjects With Previously Untreated Extensive Stage Small-cell Lung Cancer	Onyx Therapeutics, Inc.	Phase 1|Phase 2	Treatment
NCT01999881	Impacts of Exercise on Prognostic Biomarkers in Lung Cancer Patients	University of Wisconsin, Madison	not applicable	Supportive Care
NCT02011087	Bioelectrical Impedance Phase Angle in Predicting Treatment Outcome in Patients With Extensive Stage Small Cell Lung Cancer Receiving First-Line Chemotherapy	Comprehensive Cancer Center of Wake Forest University	not applicable	Diagnostic
NCT02034123	Investigation of GSK2879552 in Subjects With Relapsed/Refractory Small Cell Lung Carcinoma	GlaxoSmithKline	Phase 1	Treatment
NCT02038647	Phase 2 Study of Alisertib (MLN8237) in Combination With Paclitaxel Versus Placebo in Combination With Paclitaxel as Second Line Therapy for Small Cell Lung Cancer (SCLC)	Millennium Pharmaceuticals, Inc.	Phase 2	Treatment
NCT02062632	Doxepin Hydrochloride in Treating Esophageal Pain in Patients With Thoracic Cancer Receiving Radiation Therapy to the Thorax With or Without Chemotherapy	Mayo Clinic	not applicable	Supportive Care

NCT Number	Title	Sponsor	Phases	Primary Purpose
NCT02109016	A Study to Assess the Efficacy and Safety of the VEGFR-FGFR Inhibitor, Lucitanib, Given to Patients With Advanced/Metastatic Lung Cancer and FGF, VEGF, or PDGF Related Genetic Alterations	Clovis Oncology, Inc.	Phase 2	Treatment
NCT02161419	RONICICLIB / Placebo in Combination With Chemotherapy in Small Cell Lung Cancer	Bayer	Phase 2	Treatment
NCT02194049	Cisplatin, Etoposide and PI3K Inhibitor BKM120 in Treating Patients With Advanced Solid Tumors or Small Cell Lung Cancer	University of California, Davis	Phase 1	Treatment
NCT02200757	Efficacy and Safety of Aldoxorubicin Compared to Topotecan in Subjects With Metastatic Small Cell Lung Cancer	CytRx	Phase 2	Treatment
NCT02247349	BMS-986012 in Relapsed/Refractory SCLC	Bristol-Myers Squibb	Phase 1|Phase 2	Treatment
NCT02261805	A Phase I/II Study of Ganetespib in Combination With Doxorubicin	Georgetown University	Phase 1|Phase 2	Treatment
NCT02289690	Dose Escalation and Double-blind Study of Veliparib in Combination With Carboplatin and Etoposide in Treatment-naive Extensive Stage Disease Small Cell Lung Cancer	AbbVie	Phase 1	Treatment

NCT Number	Title	Sponsor	Phases	Primary Purpose
NCT02312622	Phase II Etirinotecan Pegol in Refractory Brain Metastases & Advanced Lung Cancer / Metastatic Breast Cancer	Stanford University	Phase 2	Treatment
NCT02351505	Selinexor in Treating Patients With Relapsed Small Cell Lung Cancer	Ohio State University Comprehensive Cancer Center	Phase 2	Treatment
NCT02359019	Pembrolizumab in Treating Patients With Extensive Stage Small Cell Lung Cancer After Completion of Combination Chemotherapy	Barbara Ann Karmanos Cancer Institute	Phase 2	Treatment
NCT02394548	Phase I Trial Of IMRT Using A Contralateral Esophagus Sparing Technique (CEST) In Locally Advanced Lung Cancer	Massachusetts General Hospital	Phase 1	Treatment
NCT02402920	Phase I Trial of MK-3475 and Concurrent Chemo/Radiation for the Elimination of Small Cell Lung Cancer	M.D. Anderson Cancer Center	Phase 1	Treatment
NCT02425072	NovoTTF-100A Therapy for Refractory CNS Involved Small Cell Lung Cancer	University of Kentucky	Phase 2	Treatment
NCT02446704	Study of Olaparib and Temozolomide in Patients With Recurrent Small Cell Lung Cancer Following Failure of Prior Chemotherapy	Massachusetts General Hospital	Phase 1|Phase 2	Treatment
NCT02481830	Efficacy Study of Nivolumab or Chemotherapy in Subjects With Relapsed Small-cell Lung Cancer	Bristol-Myers Squibb	Phase 3	Treatment

NCT Number	Title	Sponsor	Phases	Primary Purpose
NCT02487095	Trial of Topotecan With VX-970, an ATR Kinase Inhibitor, in Small Cell Lung Cancer	National Cancer Institute (NCI)	Phase 1|Phase 2	Treatment
NCT02496585	Study to Evaluate the Efficacy and Safety of Nintedanib (BIBF 1120) + Prednisone Taper in Patients With Radiation Pneumonitis	Memorial Sloan Kettering Cancer Center	Phase 2	Treatment
NCT02498613	Cediranib Maleate and Olaparib in Treating Patients With Solid Tumors That Are Metastatic or Cannot Be Removed by Surgery	National Cancer Institute (NCI)	Phase 2	Treatment
NCT02499770	G1T28 (CDK 4/6 Inhibitor) in Combination With Etoposide and Carboplatin in Extensive Stage Small Cell Lung Cancer (SCLC)	G1 Therapeutics, Inc.	Phase 1|Phase 2	Treatment
NCT02500914	SC-002 in Small Cell Lung Cancer and Large Cell Neuroendocrine Carcinoma	Stemcentrx	Phase 1	Treatment
NCT02514447	Study of G1T28 in Patients With Previously Treated Extensive Stage SCLC Receiving Topotecan Chemotherapy	G1 Therapeutics, Inc.	Phase 1|Phase 2	Treatment
NCT02538666	A Randomized, Multicenter, Double-Blind, Phase 3 Study of Nivolumab, Nivolumab in Combination With Ipilimumab, or Placebo as Maintenance Therapy in Subjects With Extensive-Stage Disease Small Cell Lung Cancer (ED-SCLC) After Completion of Platinum-based First Line Chemotherapy	Bristol-Myers Squibb	Phase 3	Treatment

NCT Number	Title	Sponsor	Phases	Primary Purpose
NCT02623712	Lung Nodule Surveillance Trial	Kaiser Permanente	not applicable	Diagnostic
NCT02628067	Study of Pembrolizumab (MK-3475) in Participants With Advanced Solid Tumors (MK-3475-158/KEYNOTE-158)	Merck Sharp & Dohme Corp.	Phase 2	Treatment
NCT02635009	Whole-Brain Radiation Therapy With or Without Hippocampal Avoidance in Treating Patients With Limited Stage or Extensive Stage Small Cell Lung Cancer	NRG Oncology Group	Phase 2|Phase 3	Treatment
NCT02661100	A Trial of CDX-1401 in Combination With Poly-ICLC and Pembrolizumab, in Previously Treated Advanced Solid Tumor Patients	Case Comprehensive Cancer Center	Phase 1|Phase 2	Treatment
NCT02674568	Study of Rovalpituzumab Tesirine (SC16LD6.5) for Third-line and Later Treatment of Subjects With Relapsed or Refractory Delta-Like Protein 3-Expressing Small Cell Lung Cancer (TRINITY)	Stemcentrx	Phase 2	Treatment